

Phthalates and Autistic Traits: Exploring the Association between Prenatal Exposures and Child Behavior

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<https://doi.org/10.1289/EHP7127>

Numerous studies have sought to pinpoint environmental risk factors for autism spectrum disorder (ASD), a neurodevelopmental disorder characterized by traits such as social deficits, atypical communication, and repetitive or restricted behaviors. Research to date has found evidence that both prenatal and early-life exposures to certain air pollutants,¹ pesticides,^{2,3} and phthalates^{4,5} could be involved. In a recent paper published in *Environmental Health Perspectives*, investigators reported associations between specific phthalate metabolites and autistic traits in a group of Canadian preschoolers, with additional evidence that folic acid supplementation during pregnancy may mitigate potential effects.⁶

“Our study may be the largest to date to look at autistic traits and phthalate exposures,” says lead author Youssef Oulhote, an epidemiologist at the University of Massachusetts Amherst and Harvard T.H. Chan School of Public Health. A few previous studies have turned up mixed results on phthalate exposures and presence of autistic traits or ASD diagnosis: Two previous studies found associations with prenatal or childhood exposure,^{4,5} but three others found no such evidence.^{7,8,9}

Oulhote and colleagues assessed autistic traits in 601 children whose mothers were enrolled in the longitudinal Maternal–Infant Research on Environmental Chemicals (MIREC) study in Canada. The cohort was designed to assess prenatal chemical

exposures and development in children born between 2008 and 2011. When the children were 3 or 4 years old, their parents filled out the Social Responsiveness Scale-II (SRS-2), a questionnaire used to assess traits and behaviors associated with ASD. The researchers investigated relationships between the children’s SRS-2 scores and concentrations of several phthalate metabolites in urine samples collected from mothers during the first trimester.

Their analysis showed that higher first-trimester concentrations of two metabolites, mono-*n*-butyl (MBP) and mono-3-carboxypropyl (MCPP), were associated with slightly higher SRS-2 scores overall. However, evaluation by gender revealed that the association with MBP was limited to boys. MBP is a breakdown product of di-*n*-butyl phthalate, which is used in cosmetics, food packaging, and other consumer products.¹⁰ MCPP is a breakdown product of several phthalates that are used primarily as plasticizers.¹¹

The investigators also assessed potential effect modification among mothers who reported taking folic acid supplements in the first trimester. In contrast with the overall findings, multiple phthalate metabolites were associated with higher scores for autistic traits when restricted to women who took less than 400 µg per day (the amount recommended by the U.S. Centers



Investigators reported that mothers with higher first-trimester urinary concentrations of the phthalate metabolite MBP were slightly more likely to see autistic traits in sons at 3 or 4 years of age. However, associations with this and other metabolites were weaker in women who took the recommended amount of folic acid supplementation while pregnant. Image: © Anna Eremeev/Shutterstock.

for Disease Control and Prevention¹²), compared with those who took 400 µg or more per day.

The findings suggest that potential effects of phthalates on autistic traits might be mitigated by adequate first-trimester folic acid supplementation. There is also evidence that folic acid may help to mitigate the association between air pollutants and pesticides and ASD.^{13,14} However, much more research is needed before we have a definitive answer, says Oulhote.

The researchers were unable to investigate how levels of folic acid supplementation compared with blood concentrations of folate, and other vitamins found in prenatal supplements could have driven the association. “It is still a very open question whether folic acid has a moderating effect or if there is a mediating effect of circulating folate,” Oulhote says. “This is a potential area of future studies to investigate whether higher exposures to environmental chemicals may interfere with folate metabolism.”

Although the SRS-2 measures traits that occur on a continuum, it is not used to diagnose autism. Higher scores on the questionnaire often correlate with other scores used for ASD clinical diagnosis, says Oulhote, though it is unclear how many and which of the children in the study actually may have had autism.

The researchers based their assessment of phthalate levels on a single urinary sample taken in the first trimester. Phthalates are metabolized very rapidly in the body, and levels in urine can vary by a factor of 1,000 times or more from day to day,^{15,16} says Hyeon-Moo Shin, an epidemiologist at the University of Texas at Arlington, who was not involved in the study. That’s an important limitation, says Shin, because “we do not know whether these levels are representative of exposure throughout pregnancy.” Oulhote says that he and his colleagues hope to include second- and third-trimester urine samples in upcoming research.

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